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PATENT COOPERATION TREATY

From the
INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

To:

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RECIBIDO
08 MAYO 2006
CLARKE MODET & C.º

PCT

WRITTEN OPINION OF THE INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

(PCT Rule 66)

Date of mailing *(day/month/year)*	05.05.2006
Applicant's or agent's file reference PXWO00762/04	**REPLY DUE** within 1 month(s) from the above date of mailing

International application No.	International filing date *(day/month/year)*	Priority date *(day/month/year)*
PCT/ES2005/000002	05.01.2005	06.01.2004

International Patent Classification (IPC) or both national classification and IPC
INV. A61K31/122

Applicant
LIPOTEC, S.A. et al.

1. ☒ The written opinion established by the International Searching Authority:
   ☐ is ☒ is not
   considered to be a written opinion of the International Preliminary Examining Authority.

2. This first opinion contains indications relating to the following items:
   - ☒ Box No. I Basis of the opinion
   - ☒ Box No. II Priority
   - ☒ Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability
   - ☐ Box No. IV Lack of unity of invention
   - ☒ Box No. V Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement
   - ☐ Box No. VI Certain documents cited
   - ☐ Box No. VII Certain defects in the international application
   - ☐ Box No. VIII Certain observations on the international application

3. The applicant is hereby **invited to reply** to this opinion.

   When? See the time limit indicated above. The applicant may, before the expiration of that time limit, request this Authority to grant an extension, see Rule 66.2(e).
   How? By submitting a written reply, accompanied, where appropriate, by amendments, according to Rule 66.3. For the form and the language of the amendments, see Rules 66.8 and 66.9.
   Also: For the examiner's obligation to consider amendments and/or arguments, see Rule 66.4*bis*. For an informal communication with the examiner, see Rule 66.6. For an additional opportunity to submit amendments, see Rule 66.4.
   If no reply is filed, the international preliminary examination report will be established on the basis of this opinion.

4. The final date by which the international preliminary report on patentability (Chapter II of the PCT) must be established according to Rule 69.2 is: 06.05.2006

Name and mailing address of the international preliminary examining authority:	Authorized Officer
European Patent Office D-80298 Munich Tel. +49 89 2399 - 0 Tx: 523656 epmu d Fax: +49 89 2399 - 4465	Fayos, C Telephone No. +49 89 2399-2180

WRITTEN OPINION OF THE INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

International application No.
PCT/ES2005/000002

Box No. I Basis of the opinion

1. With regard to the **language**, this opinion has been established on the basis of:

   ☒ the international application in the language in which it was filed

   ☐ a translation of the international application into , which is the language of a translation furnished for the purposes of:
   - ☐ international search (under Rules 12.3(a) and 23.1(b))
   - ☐ publication of the international application (under Rule 12.4(a))
   - ☐ international preliminary examination (under Rules 55.2(a) and/or 55.3(a))

2. With regard to the elements of the international application, this opinion has been established on the basis of *(replacement sheets which have been furnished to the receiving Office in response to an invitation under Article 14 are referred to in this opinion as "originally filed")*:

   Description, Pages

   1-34 as originally filed

   Claims, Numbers

   1-20 as originally filed

   ☐ a sequence listing and/or any related table(s) - see Supplemental Box Relating to Sequence Listing.

3. ☐ The amendments have resulted in the cancellation of:
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

4. ☐ This opinion has been established as if (some of) the amendments had not been made, since they have been considered to go beyond the disclosure as filed, as indicated in the Supplemental Box (Rule 70.2(c)).
   - ☐ the description, pages
   - ☐ the claims, Nos.
   - ☐ the drawings, sheets/figs
   - ☐ the sequence listing *(specify)*:
   - ☐ any table(s) related to sequence listing *(specify)*:

WRITTEN OPINION OF THE INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

International application No.
PCT/ES2005/000002

Box No. II Priority

1. ☐ This opinion has been established as if no priority had been claimed due to the failure to furnish within the prescribed time limit the requested:
   ☐ copy of the earlier application whose priority has been claimed (Rule 66.7(a)).
   ☐ translation of the earlier application whose priority has been claimed (Rule 66.7(b)).

2. ☐ This opinion has been established as if no priority had been claimed due to the fact that the priority claim has been found invalid (Rule 64.1). Thus for the purposes of this opinion, the international filing date indicated above is considered to be the relevant date.

3. Additional observations, if necessary:

see separate sheet

WRITTEN OPINION OF THE INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

International application No.
PCT/ES2005/000002

Box No. III Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

The questions whether the claimed invention appears to be novel, to involve an inventive step (to be non- obvious), or to be industrially applicable have not been examined in respect of:

☐ the entire international application

☒ claims Nos. 20 (industrial applicability)

because:

☒ the said international application, or the said claims Nos. 20 (industrial applicability) relate to the following subject matter which does not require an international preliminary examination (specify):

see separate sheet

☐ the description, claims or drawings *(indicate particular elements below)* or said claims Nos. are so unclear that no meaningful opinion could be formed *(specify)*:

☐ the claims, or said claims Nos. are so inadequately supported by the description that no meaningful opinion could be formed *(specify)*:

☐ no international search opinion has been established for the said claims Nos.

☐ a meaningful opinion could not be formed without sequence listing; the applicant did not, within the prescribed time limit:

☐ furnish a sequence listing on paper complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ furnish a sequence listing in electronic form complying with the standard provided for in Annex C of the Administrative Instructions, and such listing was not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ pay the required late furnishing fee for the furnishing of a sequence listing in response to an invitation under Rules 13*ter*.1(a) or (b) and 13*ter*.2.

☐ a meaningful opinion could not be formed without the tables related to the sequence listings; the applicant did not, within the prescribed time limit, furnish such tables in electronic form complying with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions, and such tables were not available to the International Preliminary Examining Authority in a form and manner acceptable to it.

☐ the tables related to the nucleotide and/or amino acid sequence listing, if in electronic form only, do not comply with the technical requirements provided for in Annex C-*bis* of the Administrative Instructions.

☐ See supplemental sheet for further details

WRITTEN OPINION OF THE INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY

International application No.
PCT/ES2005/000002

Box No. V Reasoned statement under Rule 66.2(a)(ii) with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

1. Statement

Novelty (N)	Claims	6-20
Inventive step (IS)	Claims	6-20
Industrial applicability (IA)	Claims	20 see separate sheet

2. Citations and explanations:

see separate sheet

WRITTEN OPINION OF THE INTERNATIONAL PRELIMINARY EXAMINING AUTHORITY (SEPARATE SHEET)

International application No.

PCT/ES2005/000002

Re Item II

Priority

1- The current assessment is based on the assumption that all claims enjoy priority rights from the filing date of the priority document. It the later turns out that is not correct, the document D1 cited in the international search report could become relevant. The same applies to D5 and D6 which were not cited in the search report.

Re Item III

Non-establishment of opinion with regard to novelty, inventive step and industrial applicability

2- Claim 20 relates to subject-matter considered by this Authority to be covered by the provisions of Rule 67.1(iv) PCT. Consequently, no opinion will be formulated with respect to the industrial applicability of the subject-matter of these claims (Article 34(4)(a)(I) PCT).

Re Item V

Reasoned statement with regard to novelty, inventive step or industrial applicability; citations and explanations supporting such statement

3- Reference is made to the following documents:

D1 US20040197282

D2 JP11116470

3.1- The documents D3-D6 were not cited in the international search report. Copies of the documents are appended hereto.

D3 WO 01/03657
D4 US2002/0123516
D5 WO2005/077111
D6 WO2005/079775

NOVELTY - Art. 33 (1) and (2) PCT

4- Claims 6-19, 20 are not novel:

4.1- D3 discloses the use of Idebenon in cosmetic as well as dermatological compositions, in amounts and in galenic forms which fall within the scope of the present claims (see D3 claims 1-15 and p 6 lines 33-39). The inhibition of melanogenesis is not mentioned. Claims 6-19 lack novelty in view of D3.

4.2- D4 discloses pharmaceutical compositions comprising idebenone. Since a composition is only defined by its components and not by its intended use or alleged effects, claims 6-8, 14, 15, 18, 19 lack novelty.

4.3- The use of idebenone for inhibiting melanogenesis is not disclosed in the available prior art.

Claim 20 does not relate to a real therapeutic use, different from that of D3. The use of claim 20 is anticipated by D3.

Hence, only claim 1-5 can be considered as being novel over the available prior art.

The applicant's attention is drawn to the fact that when / if entering the Regional phase before the EPO the present "second medical use" claims might not be acceptable under Art. 84, EPC. The therapeutic application is functionally defined by a mechanism of action which does not allow any practical application in the form of a defined, real treatment of a pathological condition (disease) (C-IV, 4.2), in line with G5/83.

INVENTIVE STEP - Art. 33 (1) and (3) PCT

5- The subject matter of claims 6-19 and 20, which is not novel, cannot be considered as being inventive.

None of the presently considered prior art documents appears to suggest the use of idebenone for inhibiting melanogenesis. This effect is shown to be achieved in the present application (examples).

The closest prior art is represented by D3.

The closest prior art differs from the present application in that it does neither mention the inhibition of melanogenesis nor the depigmentation of skin.
The technical effect achieved in the present application is shown in the examples.
The objective problem posed in the present application is to provide means for inhibiting melanogenesis and for the depigmentation of skin.
The solution proposed is the use of idebenone.
None of the presently considered prior art documents appears to suggest the use of idebenone for inhibiting melanogenesis. Claims 1-5 can presently be considered as being inventive over the available prior art documents considered.

INDUSTRIAL APPLICABILITY - Art. 33 (1) and (4) PCT

6- For the assessment of the present claim 20 on the question whether they are industrially applicable, no unified criteria exist in the PCT Contracting States. The patentability can also be dependent upon the formulation of the claims. The EPO, for example, does not recognize as industrially applicable the subject-matter of claims to the use of a compound in medical treatment, but may allow, however, claims to a known compound for first use in medical treatment and the use of such a compound for the manufacture of a medicament for a new medical treatment.

7- When / if carrying out amendments, and in order to facilitate the examination of the conformity of the amended application with the requirements of Article 34(2)(b) PCT, the applicant is requested to clearly identify the amendments carried out, no matter wether they concern amendments by addition, replacement or deletion, and to indicate precisely the passages of the application as filed on which these amendments are based (also rule 66.8 (a) PCT).

Only amendments with a clearly identified basis on the application as originally filed will be taken into account for the international preliminary examination report.